REMARKS

I. Amendments

Claims 1-9 and 14-23 have been canceled. Claims 28-51 have been added. The newly added claims do not add or constitute new matter. Support for the newly added claims may be found throughout the specification and originally filed claims.

The foregoing amendments are made solely to expedite prosecution of the instant application, and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Upon entry of the amendment, 28-51 are pending in the instant application.

II. Rejections

A. Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 3-9 and 14-23 under 35 U.S.C. 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicant respectfully traverses this rejection.

Specifically, the Examiner claims that while the specification is enabling for a female homozygous knockout mouse comprising a disruption in the PTP36 gene which results in no production of the PTP36 protein, wherein said mouse exhibits phenotypic features including androgenization, uterine abnormality, abnormal body or organ weight and abnormal physical features, as compared to a wild-type mouse, a method of producing such a transgenic mouse by homologous recombination in mouse ES cells, and a cell isolated from said female knockout mouse, it does not reasonably provide enablement for other transgenic and/or knockout animals comprising any disruption in the PTP36 gene. The Examiner further asserts that the specification is not enabling for a knockout mouse comprising any disruption in the PTP36 gene or for any cell comprising any type of disruption in a PTP36 gene, nor for a male transgenic mouse having a homozygous disruption in the PTP36 gene not exhibiting any phenotype.

In view of the cancellation of claims 3-9 and 14-23, the Examiner's rejection of these claims under 35 U.S.C. 35 U.S.C. § 112, first paragraph are moot. Therefore, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

New claims 28-51 relate to a transgenic mouse and method of producing a transgenic mouse whose genome comprises a disruption in an endogenous PTP36 gene, wherein where the mouse is female and the disruption is homozygous, the mouse lacks production of functional PTP36 protein and exhibits specific phenotypic characteristics including a uterine abnormality, a hormonal imbalance, androgenization, increased body weight, increased organ weight, reduced or absent mammary gland tissue or increased anogenital distance. Applicant submits that these claims fully meet the requirements and are patentable under 35 U.S.C. § 112, first paragraph.

B. Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1, 2, 8 and 23 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Applicant respectfully traverses this rejection.

Regarding claims 1 and 2, the Examiner asserts that the term "selectable marker" renders the claims indefinite as it is unclear how a marker protein can be part of a vector construct. The Applicant disagrees, and believes the specification has clearly defined and described the term selectable marker and how it would be used in the targeting vector. However, as these claims have been canceled, and the newly added claims recite a selectable marker gene, this aspect of the rejection is no longer relevant.

Also regarding these claims, the Examiner asserts that the arrangement of the target construct is unclear. Applicant submits that the new claims clearly set forth the relative arrangement of the elements of the targeting construct, rendering the Examiner's rejection moot.

Further, the Examiner asserts that the word "derived" renders claims 8 and 23 indefinite. Applicant respectfully disagrees. As can be found, for example, on page 2, lines 22-23 of the instant specification, the term "derived" is clearly defined and therefore not indefinite. Further, one of ordinary skill in the art would know to what the term "derived", in the context of cells and tissues "derived" from a transgenic mouse, relates. In any case, the current claims do not use the term "derived." Newly added claims use the term "obtained," which term is clear and definite. Therefore, the Examiner's rejection is no longer relevant.

Applicant submits that new claims 28-51 are definite and particularly point out and distinctly claim the subject matter regarded as the invention in accordance with 35 U.S.C. § 112, second paragraph.

C. Rejection under 35 U.S.C. § 103

Claims 1-9 are rejected by the Examiner as being unpatentable under 35 U.S.C. § 103(a) based upon the teachings of Mansour *et al.*, 1988, *Nature* 336(24):348-352 ("Mansour"), in view of Sawada *et al.*, 1994, *Biochem Biophsy Res Comm* 203(1):479-484 ("Sawada") and further in view of Ogata *et al.*, 1999, *J. Biol Chem.* 274(18):12905-12909 ("Ogata"). Applicant respectfully traverses this rejection.

Mansour describes a general approach for isolating embryonic stem cells containing a targeted mutation in a gene, provided that a cloned fragment of the gene is available. Specifically, Mansour teaches the targeted disruption of the *hprt* gene and the proto-oncogene *int*-2 in mouse embryo-derived stem cells by homologous recombination using targeting constructs pRV9.1/TK and pINT-2-N/TK, respectively. The Examiner concedes, however, that Mansour does not teach how to make an PTP36 targeting construct and knockout mouse.

According to the Examiner, Sawada discloses the cloning and characterization of a novel non-receptor protein tyrosine phosphatase (PTP36) from murine thymus. Sawada provide the nucleic acid sequence encoding PTP36.

Ogada relates to overexpression of PTP36 in HeLa cells and the effect of the overexpression on cell adhesion, cell growth and cytoskeletons. Ogada disclose that induction of PTP36 overexpression in HeLa cells resulted in cells to spread less well, grow more slowly and adhere to the extracellular matrix proteins less well than in uninduced cells, and further disclosed decreases in the actin stress fibers and number of focal adhesions in these cells. Ogada suggests a role for PTP36 in the regulation of these processes.

As a basis of the obviousness rejection under 35 U.S.C. § 103, the Examiner asserts that the ordinary artisan would have been motivated to make a PTP36 knockout construct and a transgenic knockout mouse in order to study the precise role PTP36 plays in the regulation of cell growth, adhesion and cytoskeleton. The Examiner further asserts that the ordinary artisan would have had a reasonable expectation of success because of the teachings of Mansour, Sawada and Ogata in light of the high level of skill in the art of making gene targeting constructs

and subsequently generating a knockout mouse. The Applicant respectfully disagrees. However, in light of the cancellation of claims 1-9, the rejection is no longer relevant.

Claims 29-51 relate to a transgenic mouse and method of producing a transgenic mouse whose genome comprises a disruption in an endogenous PTP36 gene, wherein where the mouse is female and the disruption is homozygous, the mouse lacks production of functional PTP36 protein and exhibits specific phenotypic characteristics including a uterine abnormality, a hormonal imbalance, androgenization, increased body weight, increased organ weight, reduced or absent mammary gland tissue or increased anogenital distance, none of which are obvious in view of the sole or combined teachings of the cited references.

As the rejection under 35 U.S.C. § 103 is no longer relevant, and new claims 28-51 are not obvious in view of the sole or combined teachings of Mansour, Sawada and/or Ogata, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 103.

It is believed that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-758.

Respectfully submitted,

Date: 10/1/03

Kelly L. Quast, Reg. No. 52,141

Deltagen, Inc.
700 Bay Road
Redwood City, CA 94063
(650) 569-5100